

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/368,670

wherein R_{11a} is H; C_{1-10} alkyl; C_6 aryl; C_{7-10} alkylaryl; C_{3-7} cycloalkyl or C_{4-8} (alkylcycloalkyl) optionally substituted with carboxyl; or heterocycle- C_{1-6} alkyl;

and R_{11b} is C_{1-6} alkyl substituted with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl; or C_{7-16} aralkyl substituted on the aromatic portion with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl;

or R_{11a} and R_{11b} are joined to form a 3 to 7-membered nitrogen-containing ring optionally substituted with carboxyl or (C_{1-6} alkoxy) carbonyl;

or

b) when Q is N-Y, a is 0 or 1, b is 0 or 1, and

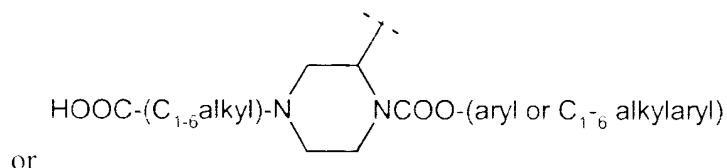
B is H, an acyl derivative of formula $R_{11}-C(O)-$ or a sulfonyl of formula $R_{11}-SO_2$ wherein

R_{11} is (i) C_{1-10} alkyl optionally substituted with carboxyl or C_{1-6} alkanoyloxy; C_{1-6} alkoxy; or carboxyl substituted with 1 to 3 C_{1-6} alkyl substituents;

(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, both optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl;

(iii) C_6 or C_{10} aryl or C_{7-16} aralkyl optionally substituted with C_{1-6} alkyl, hydroxy, or amino optionally substituted with C_{1-6} alkyl; or

(iv) Het optionally substituted with C_{1-6} alkyl, hydroxy, amino optionally substituted with C_{1-6} alkyl, or amido optionally substituted with C_{1-6} alkyl,



R_6 , when present, is C_{1-6} alkyl substituted with carboxyl;

R_5 , when present, is C_{1-6} alkyl optionally substituted with carboxyl;

and

c) when Q is either CH_2 or N-Y, then

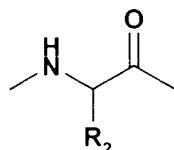
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R₄ is C₁₋₁₀ alkyl, C₃₋₇ cycloalkyl or C₄₋₁₀ (alkylcycloalkyl);

z is oxo or thioxo;

R₃ is C₁₋₁₀ alkyl optionally substituted with carboxyl, C₃₋₇ cycloalkyl or C₄₋₁₀ (alkylcycloalkyl);

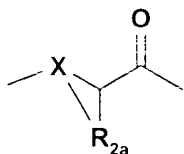
W is a group of formula II:



Formula II

wherein R₂ is C₁₋₁₀ alkyl or C₃₋₁₀ cycloalkyl optionally substituted with carboxyl or an ester or amide thereof; C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl; or

W is a group of formula IIa:



Formula IIa

wherein X is CH or N; and

R_{2a} is divalent C₃₋₄ alkylene which together with X and the carbon atom to which X and R_{2a} are attached form a 5- or 6-membered ring, said ring optionally substituted with OH; SH; NH₂; carboxyl; R₁₂; CH₂-R₁₂, OR₁₂, C(O)OR₁₂, SR₁₂, NHR₁₂ or NR₁₂R_{12a}[:];

wherein R₁₂ and R_{12a} are independently a saturated or unsaturated C₃₋₇ cycloalkyl or C₄₋₁₀ (alkyl cycloalkyl) being optionally mono-, di- or tri-substituted with R₁₅,

or R₁₂ and R_{12a} is a C₆ or C₁₀ aryl or C₇₋₁₆ aralkyl optionally mono-, di- or tri-substituted with R₁₅, or R₁₂ and R_{12a} is Het or (lower alkyl)-Het optionally mono-, di- or tri-substituted with R₁₅.

wherein each R₁₅ is independently C₁₋₆ alkyl; C₁₋₆ alkoxy; amino optionally mono- or di-substituted with C₁₋₆ alkyl; sulfonyl; NO₂; OH; SH; halo; haloalkyl; amido optionally mono-substituted with C₁₋₆ alkyl, C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl, Het or (lower alkyl)-Het; carboxyl; carboxy(lower alkyl); C₆ or C₁₀ aryl, C₇₋₁₆ aralkyl or

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Het, said aryl, aralkyl or Het being optionally substituted with R₁₆;

wherein R₁₆ is C₁₋₆ alkyl; C₁₋₆ alkoxy; amino optionally mono- or di-substituted with C₁₋₆ alkyl; sulfonyl; NO₂; OH; SH; halo; haloalkyl; carboxyl; amide; or (lower alkyl)amide;

or X is CH or N; and R_{2a} is a divalent C₃₋₄ alkylene which together with X and the carbon atom to which X and R_{2a} are attached form a 5- or 6-membered ring which in turn is fused with a second 5-, 6- or 7-membered ring to form a bicyclic system wherein the second ring is substituted with OR_{12a} wherein R_{12a} is C₇₋₁₆ aralkyl;

R_{1a} is hydrogen, and R₁ is the side chain of an amino acid selected from the group consisting of cysteine (Cys), aminobutyric acid (Abu), norvaline (Nva) and allylglycine (AlGly); or

R_{1a} and R₁ together form a 3- to 6-membered ring optionally substituted with R₁₄ wherein R₁₄ is C₁₋₆ alkyl, C₃₋₅ cycloalkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₆ aryl or C₇₋₁₀ aralkyl all optionally substituted with halo; and

A is hydroxy [or a pharmaceutically acceptable salt of ester thereof]; or C₁₋₆ alkylamino, di(C₁₋₆ alkyl)amino or phenyl-C₁₋₆ alkylamino;

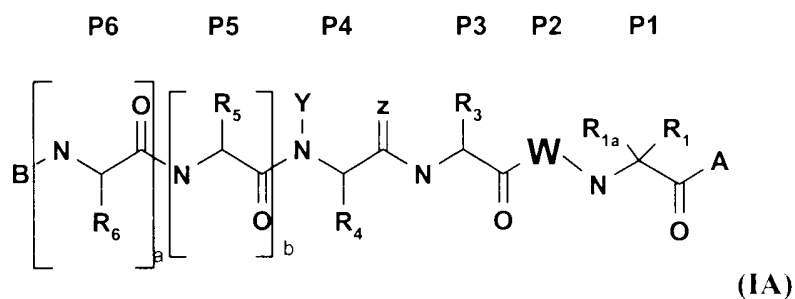
or a pharmaceutically acceptable salt or ester thereof.

Claim 23, line 7 (page 153, line 4), after "position with" insert --R₁₃, wherein --;
line 8 (page 153, line 5), after "or 2, and" delete -- R₁₃, wherein --.

Claim 32, line 3, delete "all of which" and insert --each of which is--.

40. (Amended) A compound of formula (IA) [including] or the racemates, diastereoisomers [and] or optical isomers thereof

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wherein Y is H or C₁₋₆ alkyl;

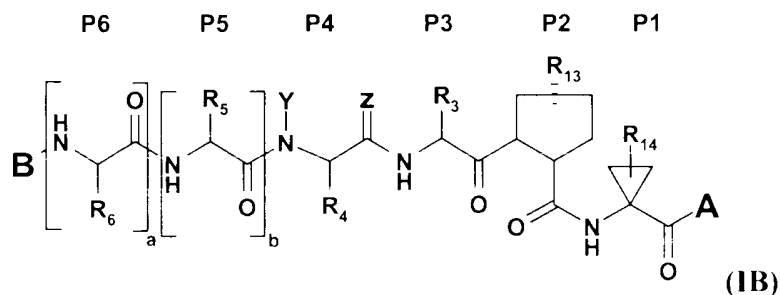
a is 0 or 1;

b is 0 or 1;

B is as defined in claim 1, paragraph b);

R₆, R₅, R₄, Z, R₃, W, R₁, R_{1a} and A are as defined in claim 1.

45. (Amended) A compound of formula IB [including] or the racemates, diastereoisomers [and] or optical isomers thereof:



wherein

B, a, b, R₆, R₅, Y, R₄, Z, R₃, and A are as defined in claim 1,

R₁₃ is R₁₂, OR₁₂, C(O)OR₁₂, SR₁₂, NHR₁₂ or NR₁₂, R₁₂, wherein R₁₂ and R_{12a} are as defined in claim 1; and

R₁₄ is C₁₋₆ alkyl, C₂₋₆ alkenyl optionally substituted with halogen; C₆₋₁₀ aryl or C₇₋₁₀ aralkyl optionally substituted with halogen; or a pharmaceutically acceptable salt or ester

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thereof.

6.3
Claim 54, line 2, delete "naphtylmethoxy" and insert --naphthylmethoxy--.

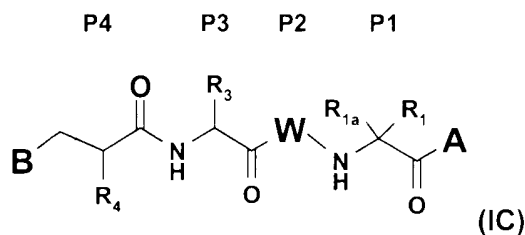
6.4
Claim 58, line 1, delete "the P1 segment" and insert --P1--.

Claims 59 and 60, line 1 of each claim, delete "said P1 segment" and insert --P1--.

Claim 61, delete "said asymmetric carbon at position 1" and insert --the C₁ carbon atom--.

Claim 63, line 2, delete "all of which" and insert --each of which is--.

67. (Amended) A compound of formula IC [including] or the racemates,
diastereoisomers [and] or optical isomers thereof:



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wherein B is as defined in claim 1, paragraph a);

R₄, R₃, W, R_{1a}, P₂, and A are as defined in claim 1.

Claim 96, line 2, delete "therapeutically" and insert --pharmaceutically--.